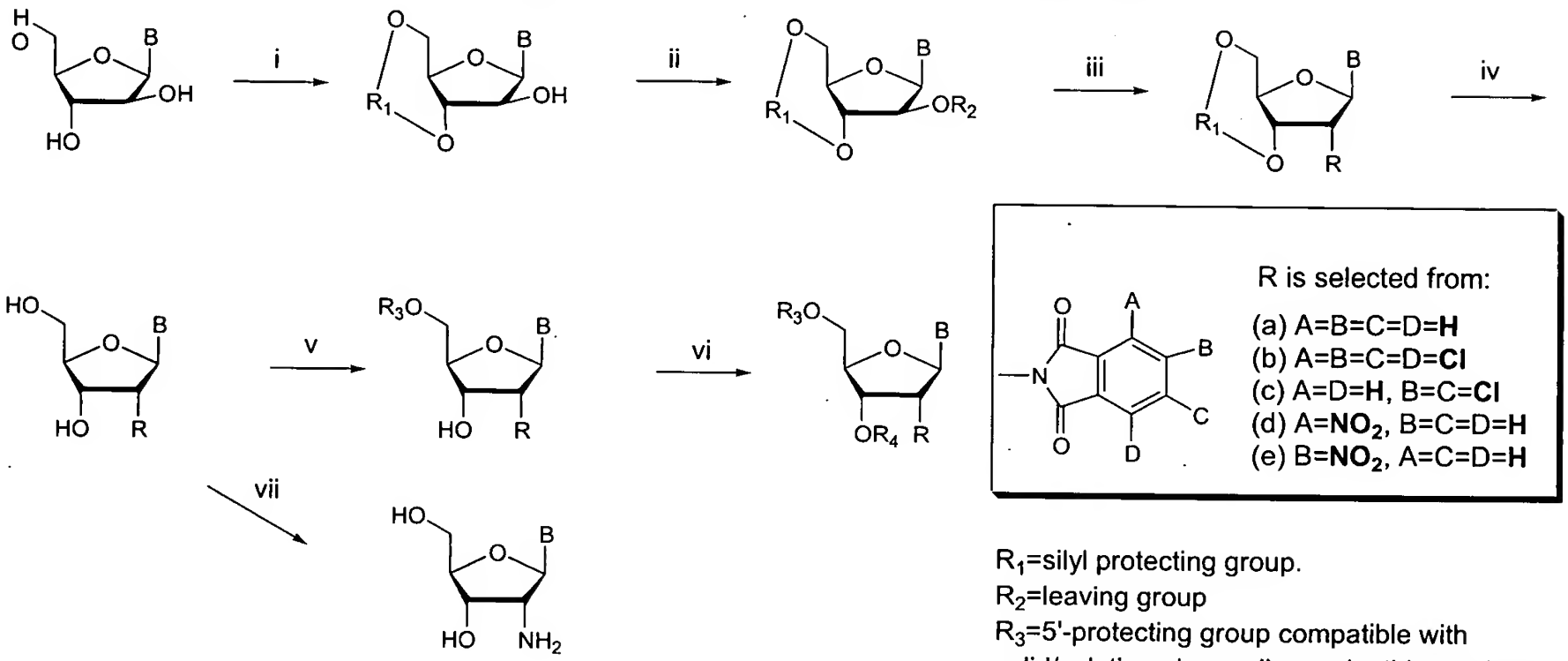
Figure 1: Synthesis of 2'-deoxy-2'-amino nucleosides, C-nucleosides and 2'-deoxy-2'-N-phthaloyl nucleoside and C-nucleoside phosphoramidites



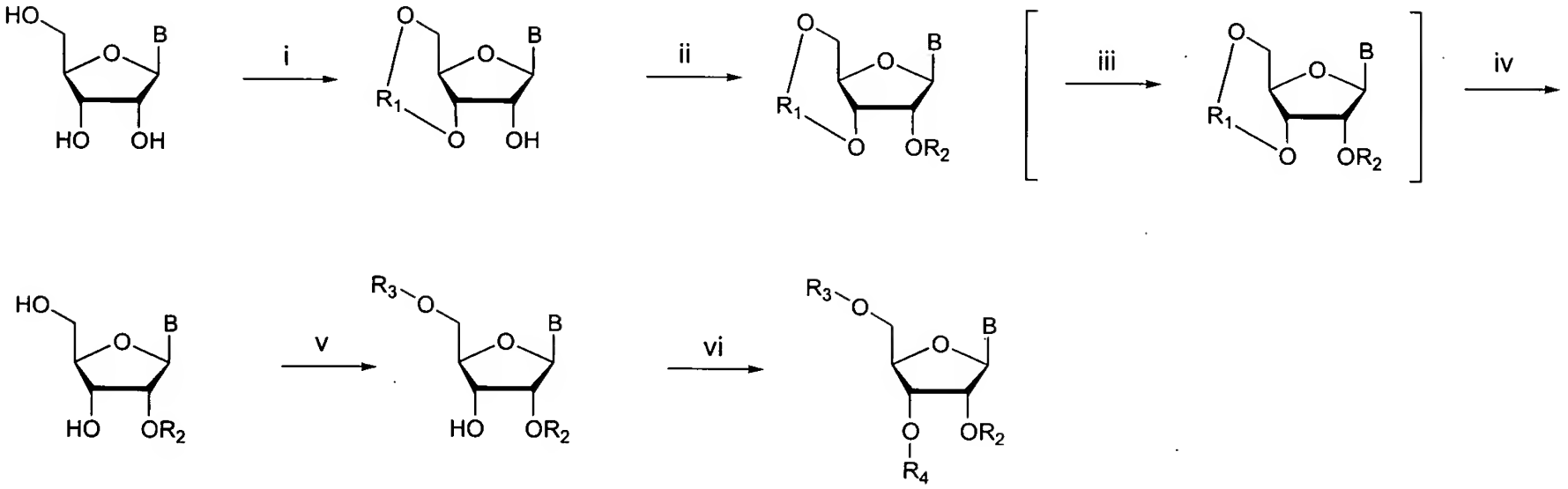
R is selected from:

(a) A=B=C=D=**H**
(b) A=B=C=D=**Cl**
(c) A=D=**H**, B=C=**Cl**
(d) A=**NO_2**, B=C=D=**H**
(e) B=**NO_2**, A=C=D=**H**

i) Simultaneous protection of 5' and 3' hydroxyls; ii) introduction of leaving group; iii) displacement of leaving group; iv) deprotection of 5' and 3'-hydroxyls; v) protection of 5'-hydroxyl; vi) phosphitylation; vii) deprotection of amine

R_1=silyl protecting group.
R_2=leaving group
R_3=5'-protecting group compatible with solid/solution phase oligonucleotide synthesis
R_4=phosphoramidite moiety
B=protected or unprotected nucleic acid base or C-glycoside aglycon

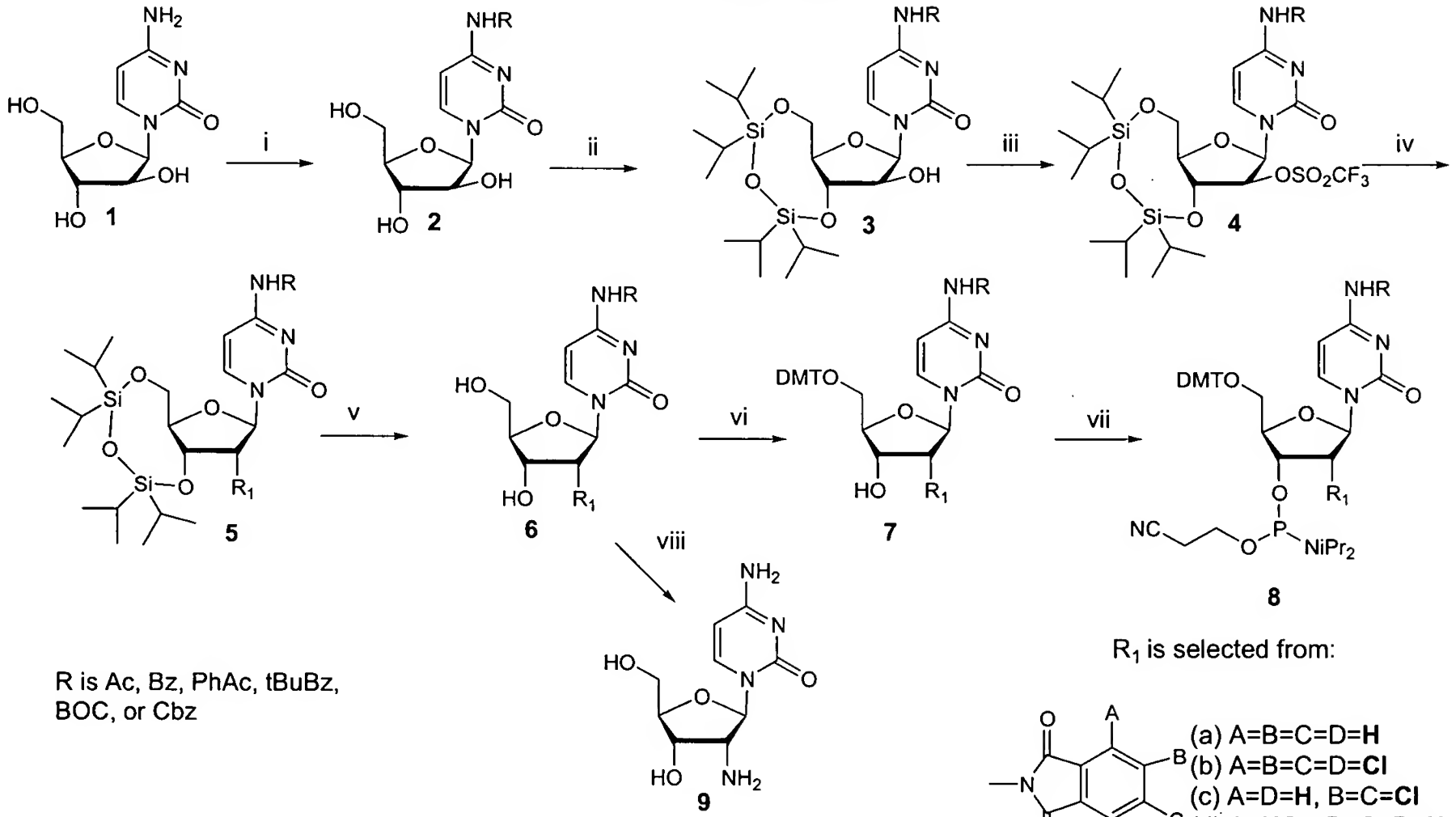
Figure 2: Synthesis of 2'-O-silyl nucleoside phosphoramidites and 2'-O-silyl C-nucleoside phosphoramidites



i) introduction of cyclic silyl protection; ii) introduction of 2'-silyl ether; iii) introduction of base protection (when necessary); iv) deprotection of 5' and 3'-hydroxyls; v) introduction of 5'-protection; vi) phosphitylation

R_1= cyclic silyl protecting group.
R_2=substituted silyl, for example tert-butyldimethylsilyl (TBDMS) or triisopropylsilyloxymethyl (TOM).
R_3=5'-protecting group compatible with solid/solution phase oligonucleotide synthesis.
R_4=phosphoramidite moiety
B=protected or unprotected nucleic acid base or C-glycoside aglycon.

Figure 3: Synthesis of 2'-deoxy-2'-N-phthaloyl Cytidine Phosphoramidite



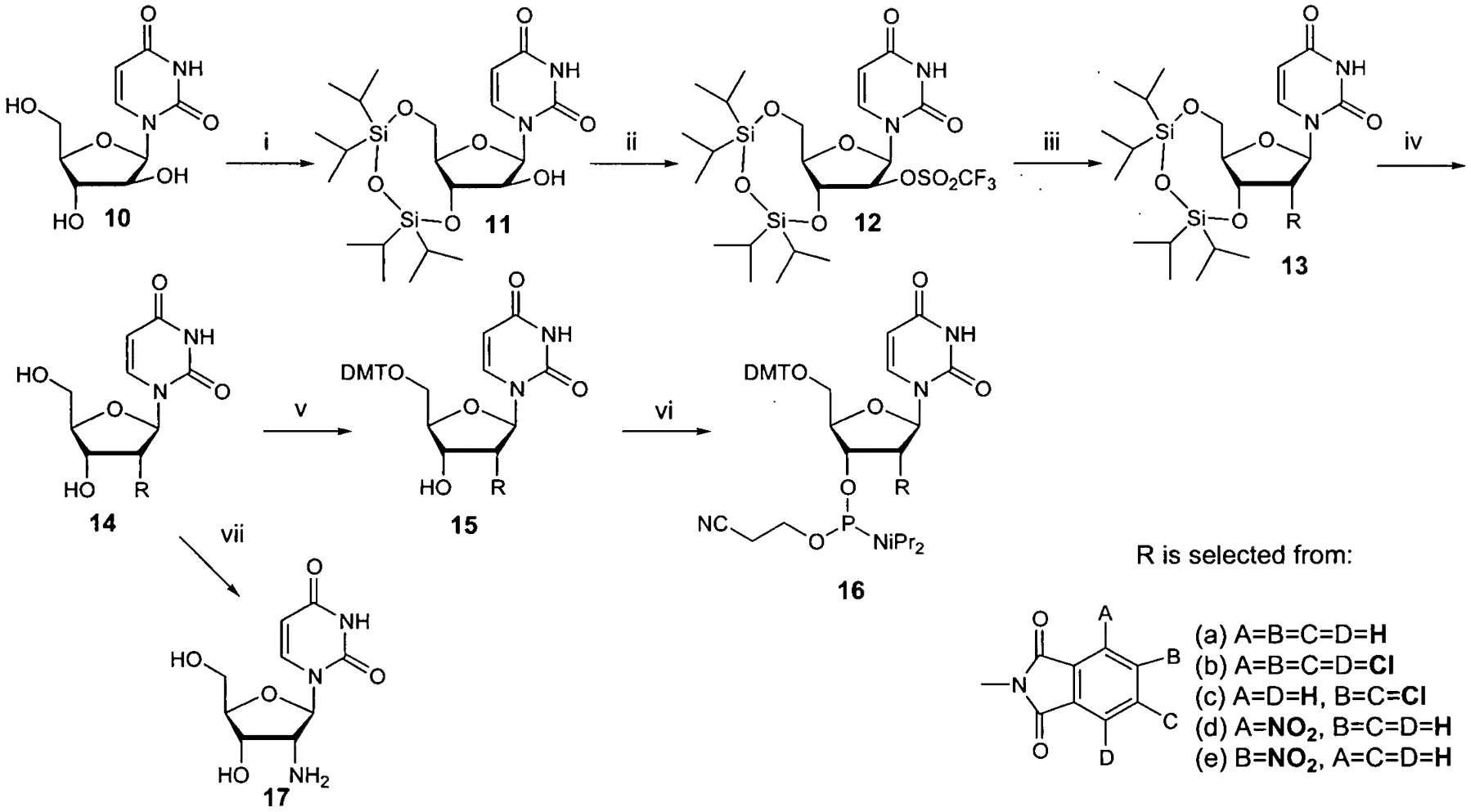
R is Ac, Bz, PhAc, tBuBz, BOC, or Cbz

R_1 is selected from:

(a) A=B=C=D=**H**
(b) A=B=C=D=**Cl**
(c) A=D=**H**, B=C=**Cl**
(d) A=**NO_2**, B=C=D=**H**
(e) B=**NO_2**, A=C=D=**H**

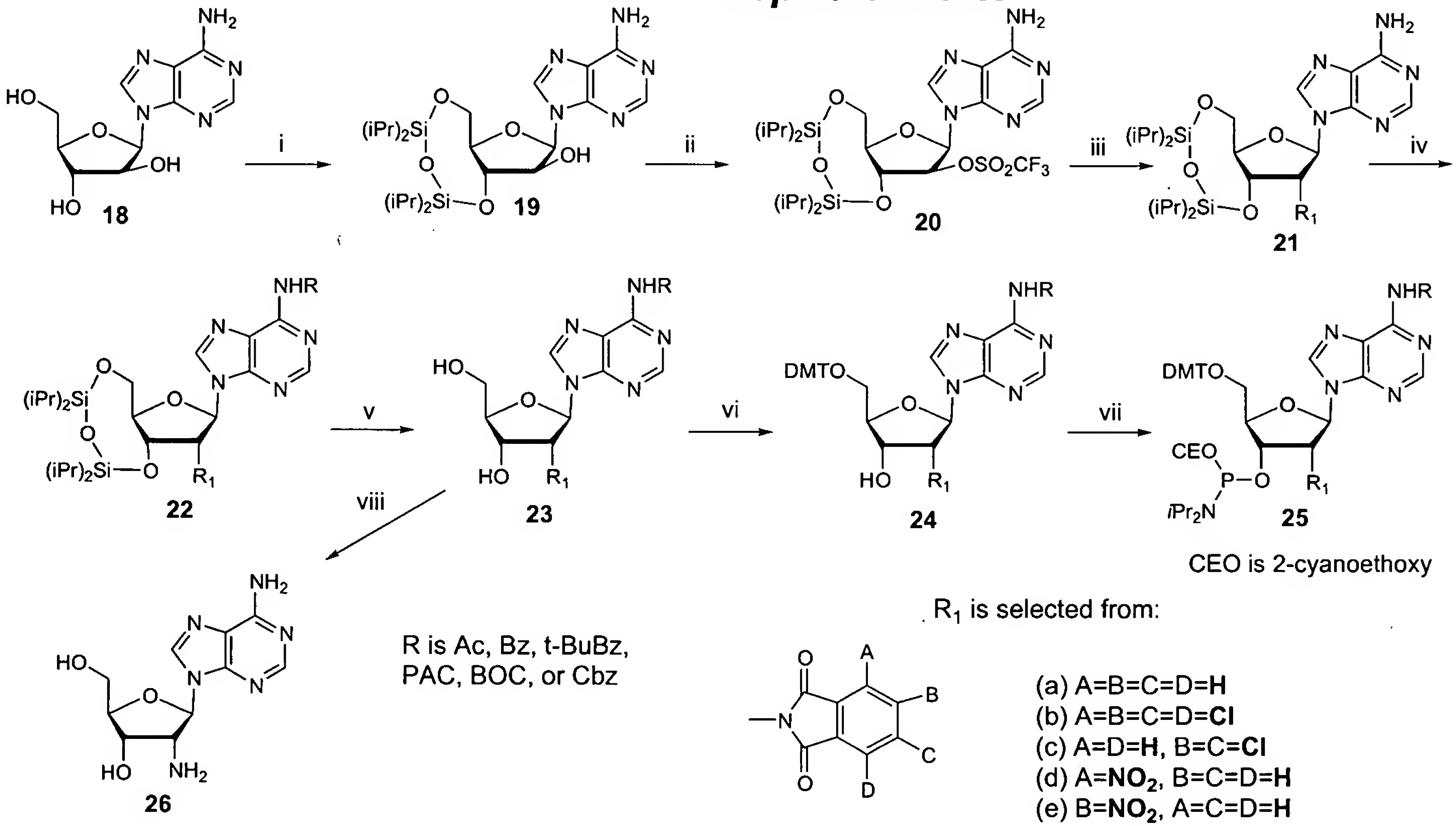
R ag nts & Conditions: i) Ac_2O/DMF; ii) TIPDSiCl/Pyr; iii) triflic anhydride, DMAP/CH_2Cl_2; iv) phthalimide or substituted phthalimide, DBU/MeCN; v) Et_3N•3HF/THF; vi) DMTCl/Pyr; vii) phosphitylation; viii) 40% aq methylamine

Figure 4: Synthesis of 2'-deoxy-2'-N-phthaloyl Uridine Phosphoramidite



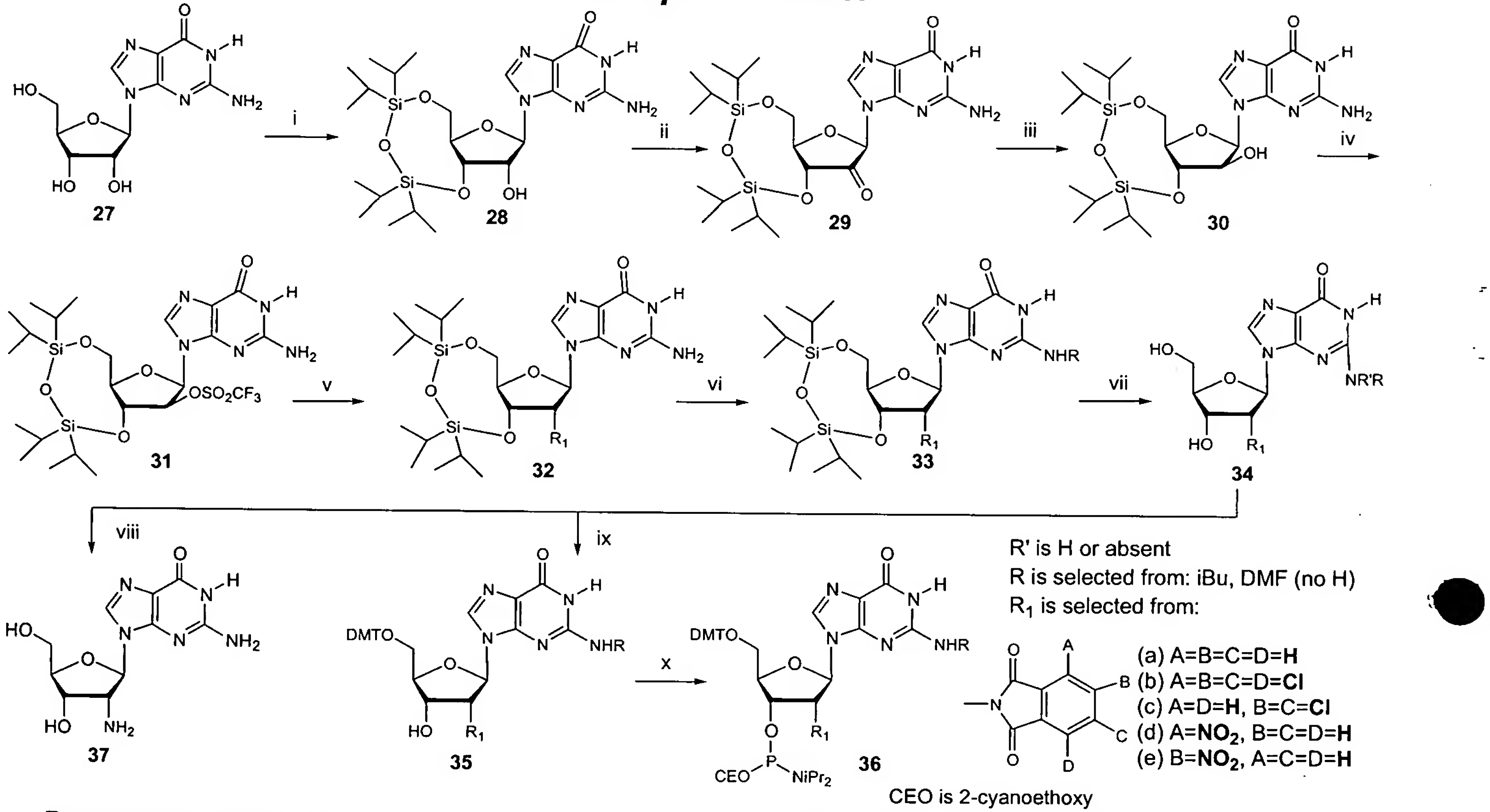
Reagents & Conditions: i) TIPDSiCl/Pyr; ii) triflic anhydride, DMAP/CH_2Cl_2; iii) phthalimide or substituted phthalimide, DBU/MeCN; iv) $ET_3N{\cdot}3HF$/THF; v) DMTCl/Pyr; vi) phosphitylation; vii) 40% aq methylamine

Figure 5: Synthesis of 2'-deoxy-2'-N-phthaloyl Adenosine Phosphoramidite



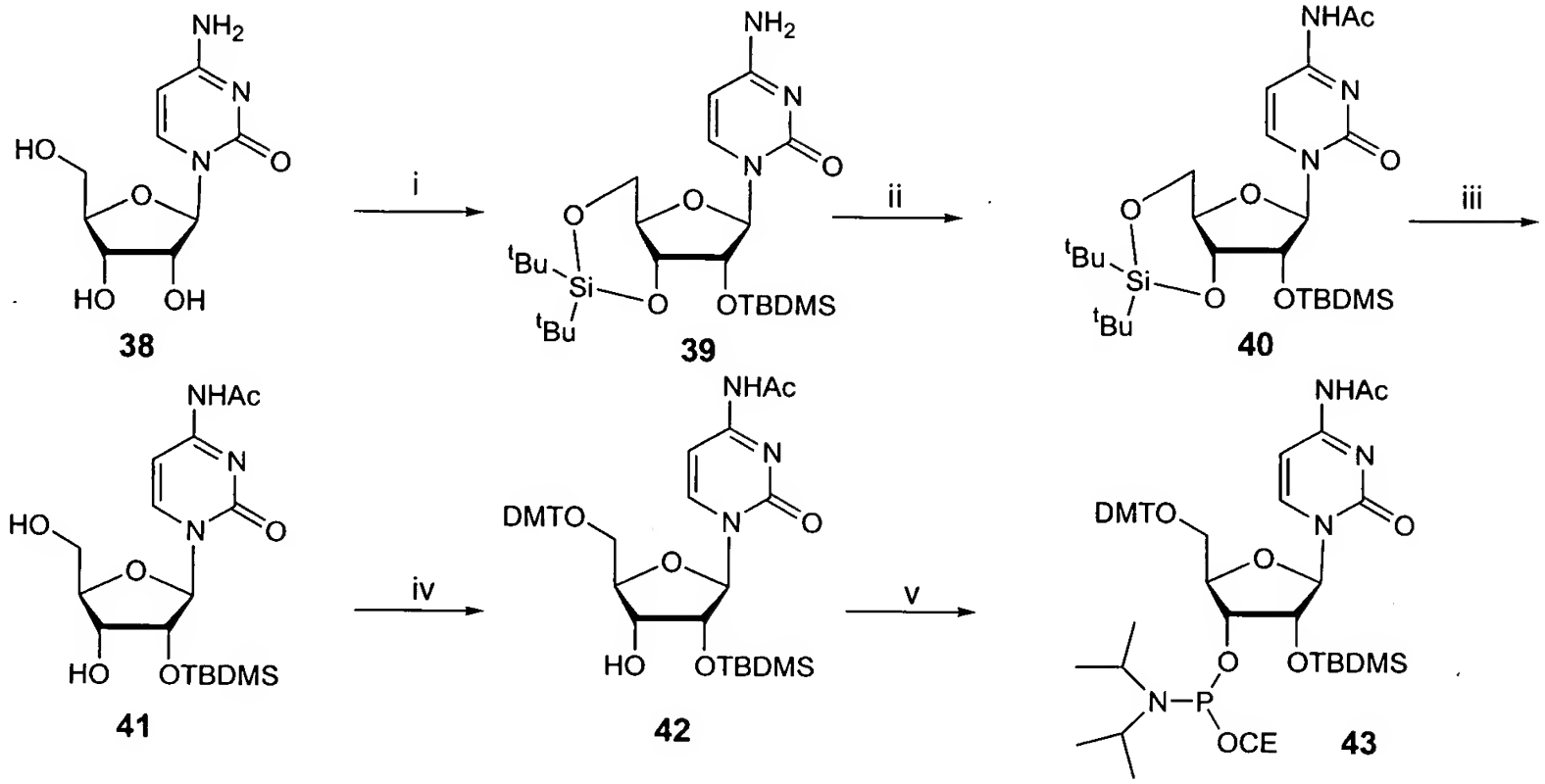
Reag nts &Conditions: i)TIPDSiCl /Pyr; ii) triflic chloride, DMAP/methylene chloride; iii) phthalimide or substituted phthalimide, DBU/MeCN; iv) Acyl chloride or anhydride/Pyr; v) Et_3N•HF/THF; vi) DMT-Cl/Pyr, 0°C; vii) phosphitylation; viii) 40% aq methylamine

Figure 6: Synthesis of 2'-deoxy-2'-N-phthaloyl Guanosine Phosphoramidite



Reagents and conditions: i) TIPDSiCl/Py; ii) CrO_3/Py/Ac_2O; iii) $NaBH_4$/EtOH; iv) CF_3SO_2Cl/CH_2Cl_2, 0°C; v) phthalimide or substituted phthalimide, DBU/MeCN; vi) isobutyryl chloride/Pyr; vii) $Et_3N{\cdot}3HF$/THF; viii) 40% aq $MeNH_2$; ix) DMT-Cl/Py; x) phosphitylation

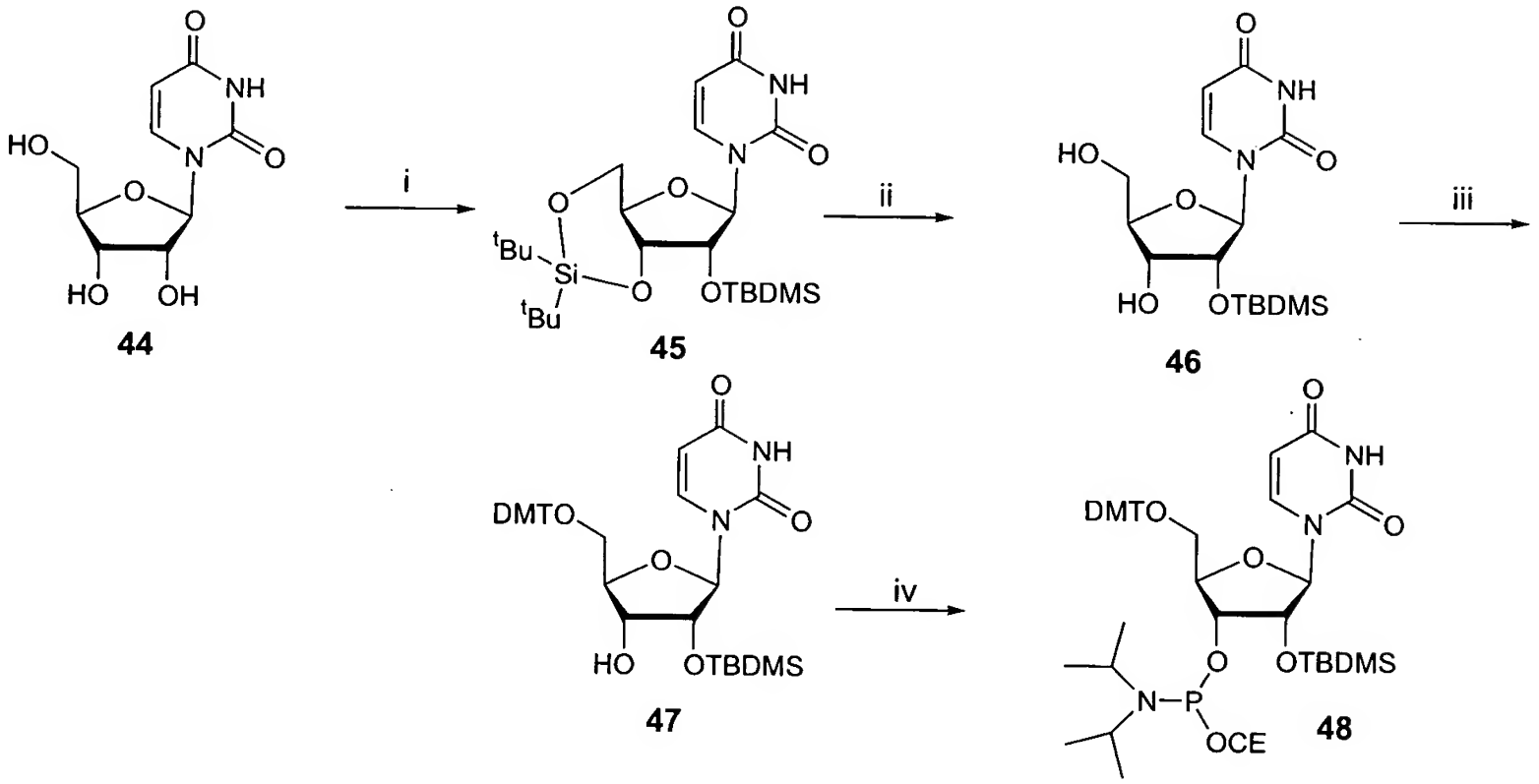
Figure 7: Synthesis of 5'-O-dimethoxytrityl-2'-O-tert-butyldimethylsilyl-N4-acetyl Cytidine 3'-O-(2-cyanoethyl-N,N-diisopropylphosphoramidite)



CE = 2-cyanoethyl

Reagents & Conditions: i) a. $MeSO_3H$; b. tert-$Bu_2Si(OSO_2CF_3)_2$ / Imidazole;
c. tert-$BuMe_2SiCl$ / Imidazole ii) acetic anhyride/pyridine iii) HF-Pyr/CH_2Cl_2; iv) DMT-Cl / Pyr; v) phosphitylation

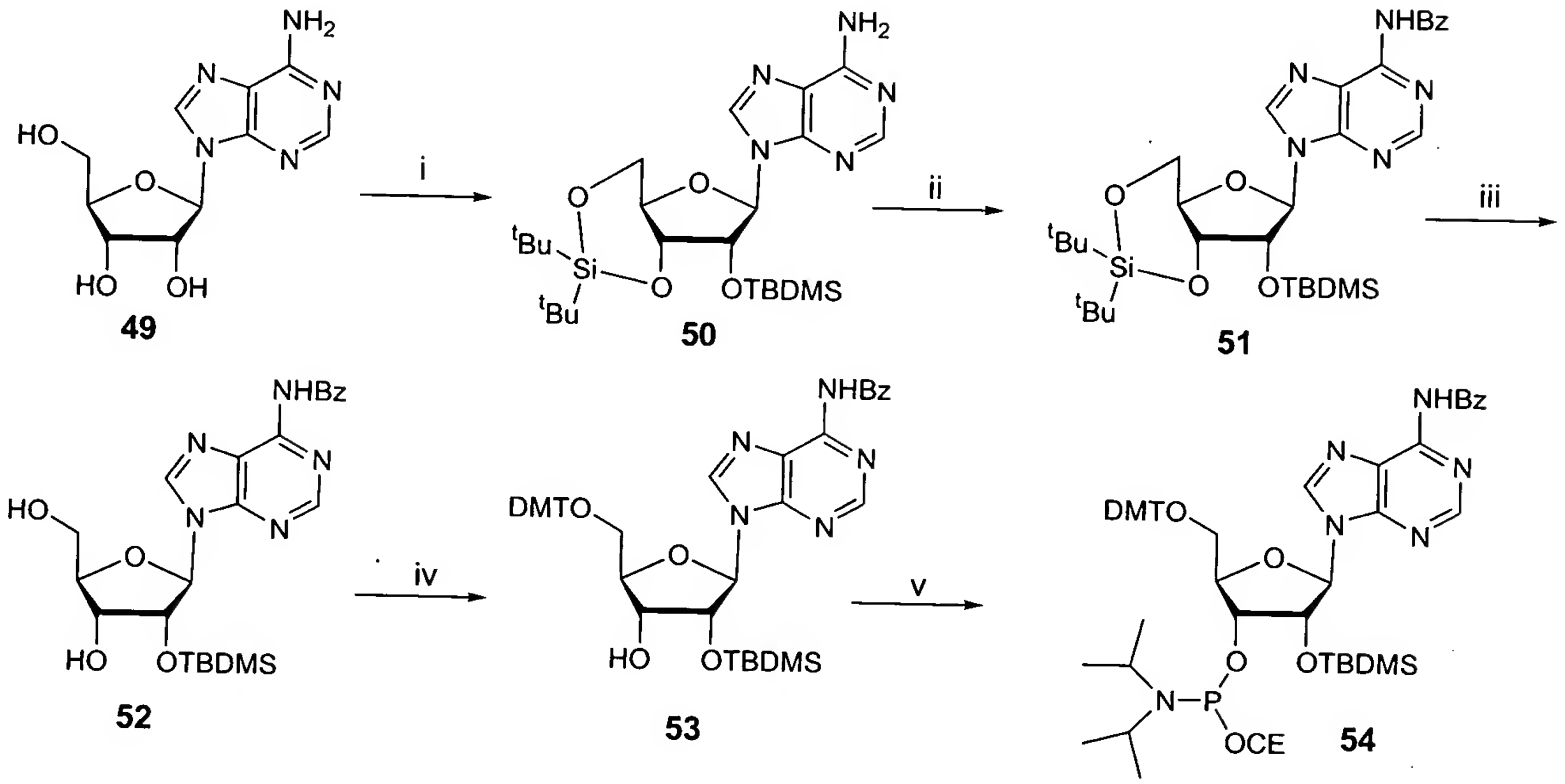
Figure 8: Synthesis of 5'-O-dimethoxytrityl-2'-O-tert-butyldimethylsilyl Uridine 3'-O-(2-cyanoethyl-N,N-diisopropylphosphoramidite)



CE = 2-cyanoethyl

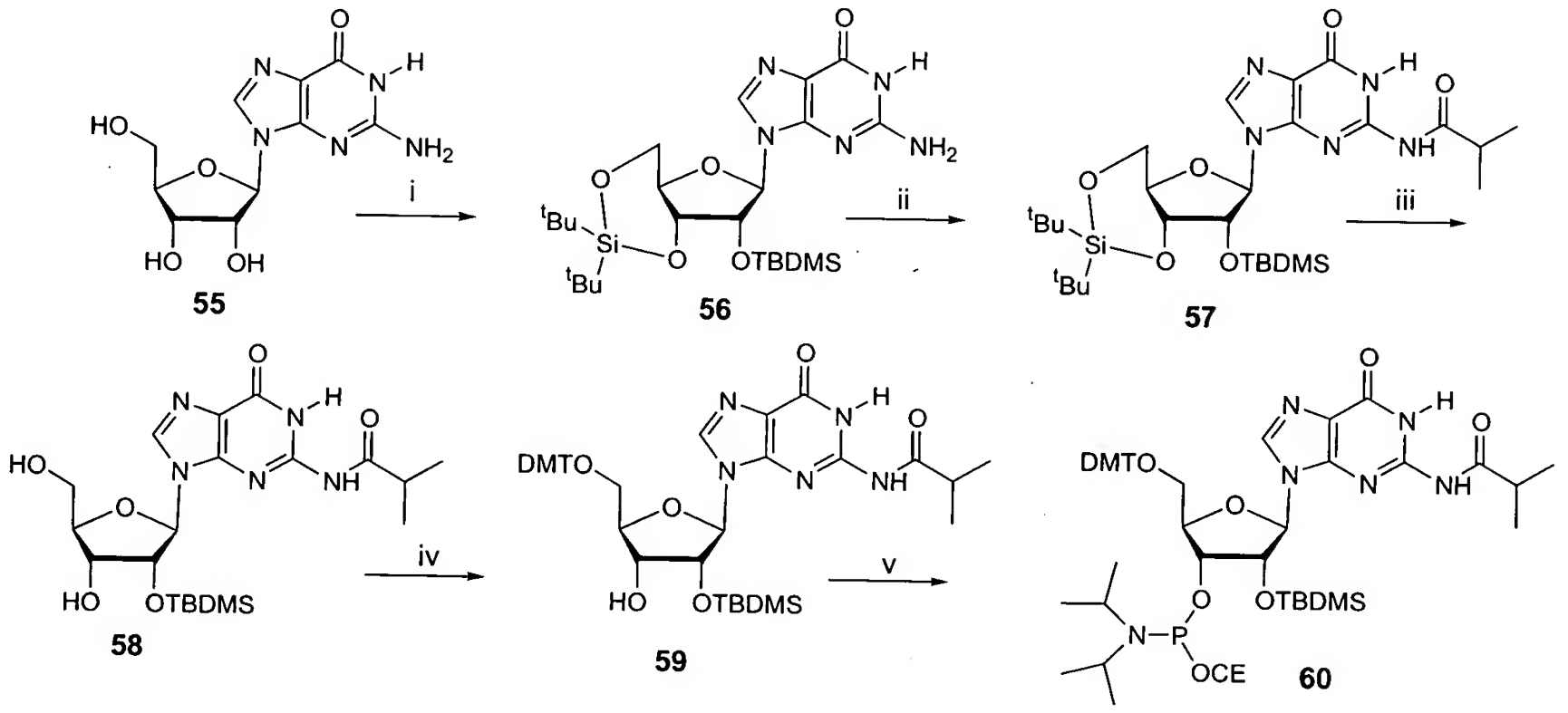
Reag nts & Conditions: i) a. tert-$Bu_2Si(OSO_2CF_3)_2$ / Imidazole,
b. tert-$BuMe_2SiCl$ / Imidazole; ii) HF-Pyr/CH_2Cl_2; iii) DMT-Cl / Pyr; iv) phosphitylation

Figure 9: Synthesis of 5'-O-dimethoxytrityl-2'-O-tert-butyldimethylsilyl-N6-benzoyl Adenosine 3'-O-(2-cyanoethyl-N,N-diisopropylphosphoramidite)



Reagents & Conditions: i) a. tert-$Bu_2Si(OSO_2CF_3)_2$ / Imidazole, b. tert-$BuMe_2SiCl$ / Imidazole; ii) a. Benzoyl chloride/Pyr b. Morpholine; iii) HF-Pyr/CH_2Cl_2; iv) DMT-Cl / Pyr; v) phosphitylation

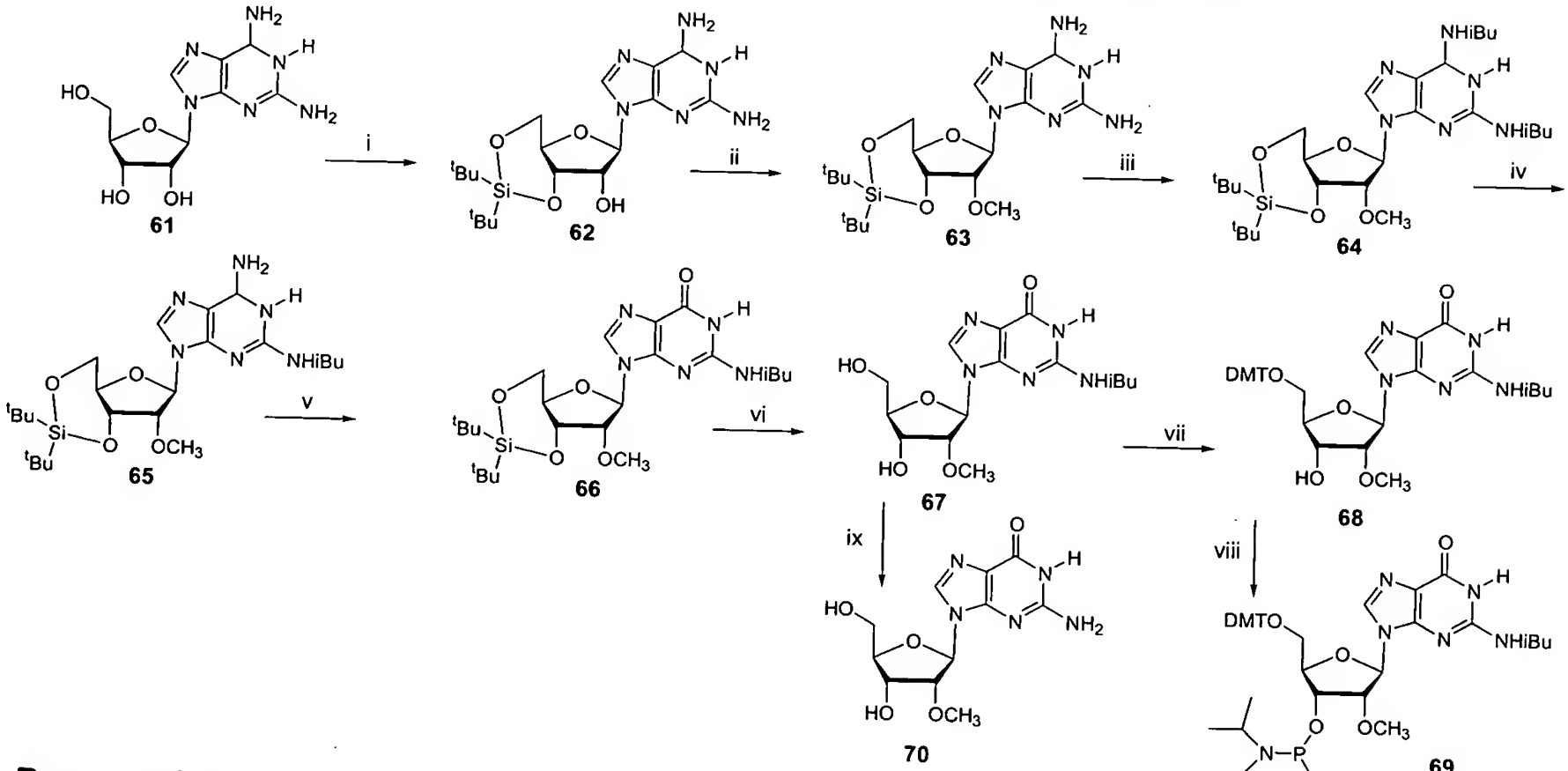
Figure 10: Synthesis of 5'-O-dimethoxytrityl-2'-O-tert-butyldimethylsilyl-N2-isobutyryl Guanosine 3'-O-(2-cyanoethyl-N,N-diisopropylphosphoramidite)



CE = 2-cyanoethyl

Reagents & Conditions: i) a. tert-$Bu_2Si(OSO_2CF_3)_2$ / Imidazole, b. tert-$BuMe_2SiCl$ / Imidazole; ii) a. Isobutyryl chloride/Pyr, b. Methylamine/EtOH; iii) HF-Pyr/CH_2Cl_2; iv) DMT-Cl / Pyr; v) phosphitylation

Figure 11: Synthesis of 2'-O-methyl Guanosine and 5'-O-dimethoxytrityl-2'-O-methyl-N2-isobutyryl Guanosine 3'-O-(2-cyanoethyl-N,N-diisopropylphosphoramidite)



Reagents & Conditions: i) tert-$Bu_2Si(OSO_2CF_3)_2$ / Imidazole; ii) MeI, NaH/DMF; iii) iBuCl/pyr; iv) Et_3N/MeOH; v) $NaNO_2$/AcOH; vi) HF-Pyr; vii) DMT-Cl / Pyr; viii) phosphitylation; ix) methylamine

Figure 12. Elimination reaction

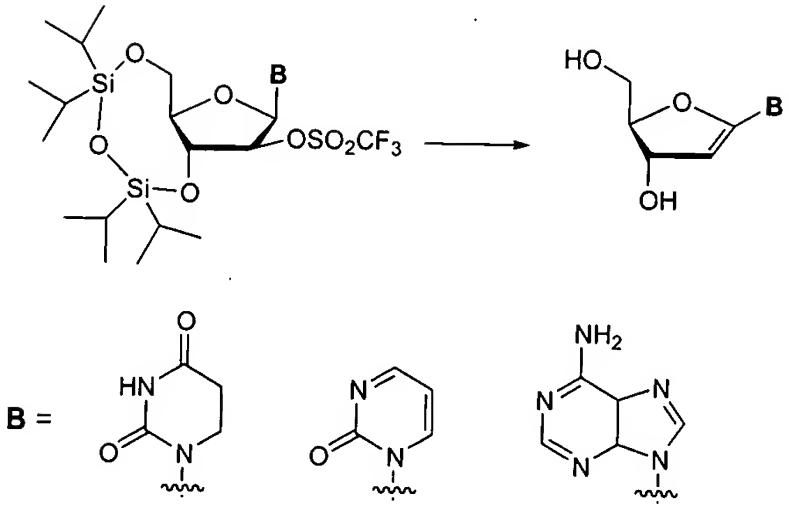


Figure 13: Synthesis of 2'-O-methyl-N6-benzoyl Adenosine Derivatives

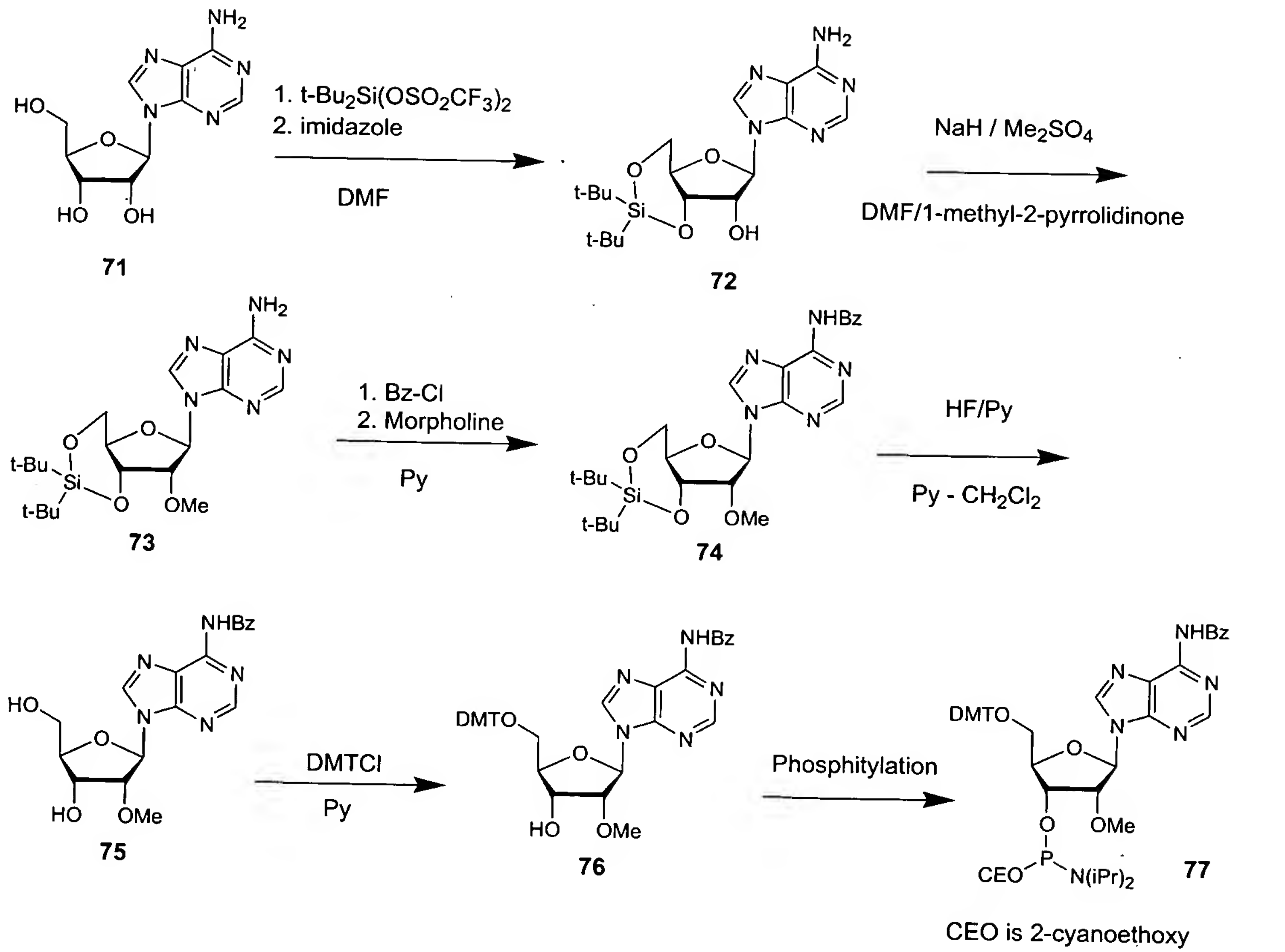


Figure 14: Synthesis of 2'-O-methyl Adenosine Derivatives

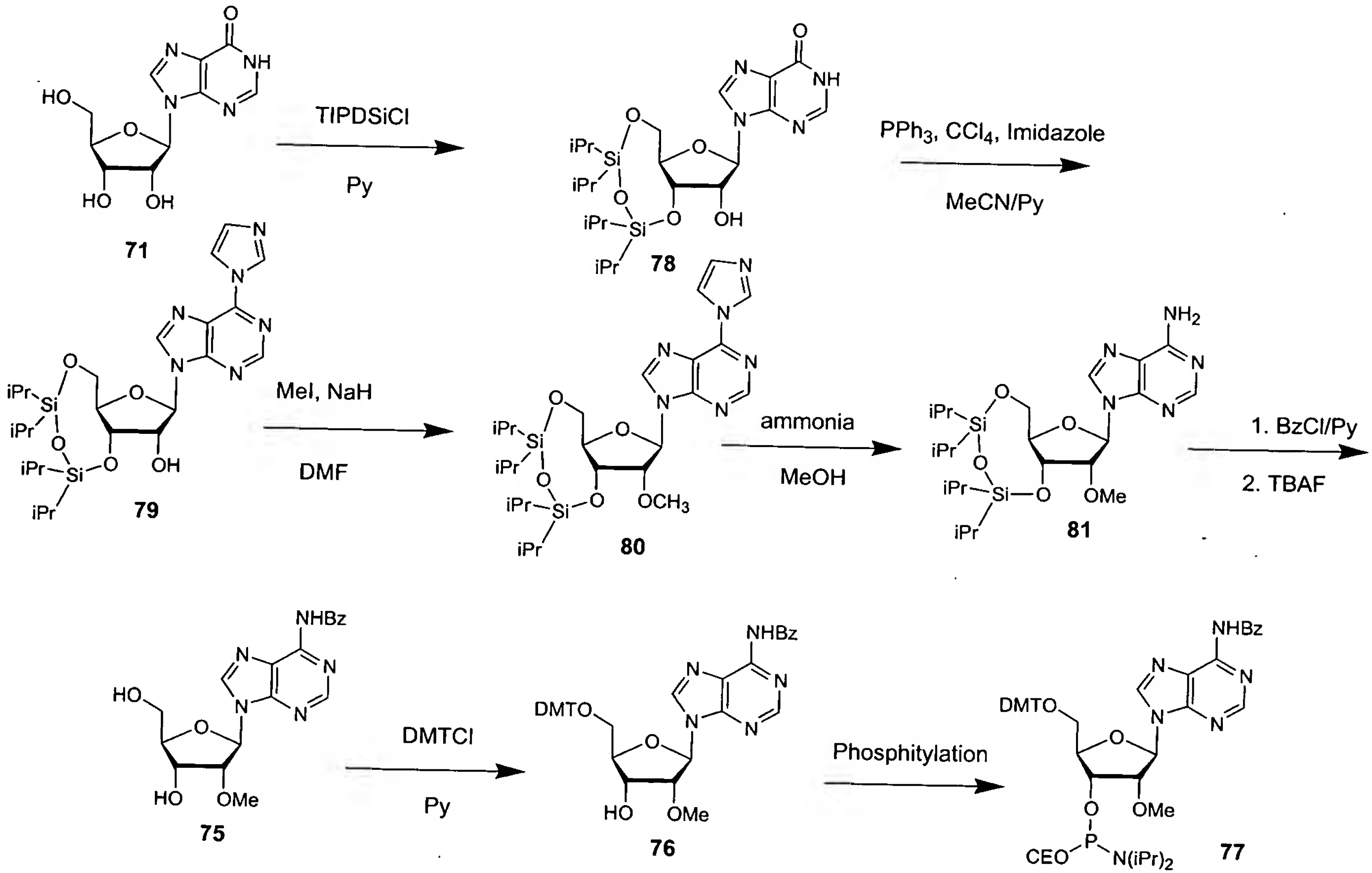
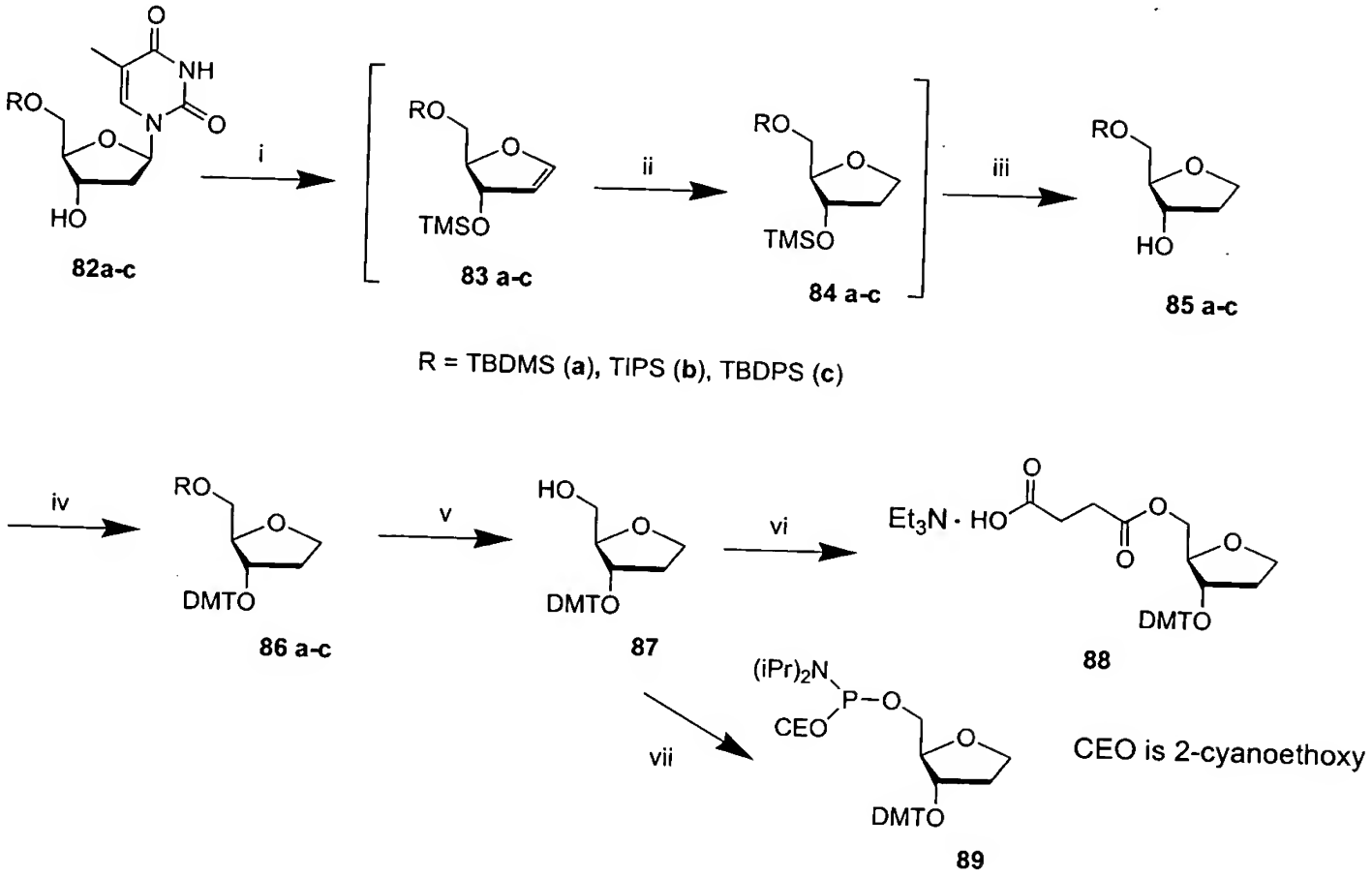


Figure 15: Synthesis of 1,4-Anhydro-2-deoxy-D-erythro-pentitol derivatives



Reagents & Conditions: i) HMDS, catalyst, reflux; ii) H_2, Pd/C; iii)Py·TFA (0.05 eq), MeOH; iv) DMT-Cl, Py, DMAP; v) NaOH, EtOH-H_2O, reflux; vi) succinic anhydride, Py, DMAP, then Et_3Nvii) phosphitylation